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# Arteriovenous Fistula: A Complication Following Renal Biopsy of Suspected Bilateral Wilms' Tumor

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**Key words:** fistula, biopsy, Wilms' tumor

### Max J. Coppes, MD, PhD (Pediatric Oncologist)

L.-A.W., a previously well, nearly 5-year-old Caucasian girl, presented with a 1-day history of macroscopic hematuria. Her past history was unremarkable; in particular, there were no other urinary symptoms such as polyuria or dysuria, no history of fever or trauma, and no abdominal pain. No abdominal mass had been noticed. Physical examination, however, revealed a large, nontender, firm mass in the left upper quadrant of the abdomen. In addition, both systolic (137 mmHg) and diastolic blood pressures (77 mmHg) were elevated. Further examination revealed no external genitourinary malformations, hemihypertrophy, or aniridia. Urinalysis confirmed the hematuria and in addition revealed a mild (+1) proteinuria. Abdominal ultrasound demonstrated a large solid inhomogeneous mass in the lower pole of the left kidney; a second mass was noted in the midportion of the right kidney. Subsequent abdominal computed axial tomography (CAT) demonstrated a $6 \times 6 \times 7$ cm mass in the lower pole of the left kidney with a tumor thrombus in the left renal vein. Within the right kidney, an isodense mass measuring ~2–3 cm was demonstrated. Finally, chest X-ray and CAT-scan of the chest revealed multiple soft tissue nodules scattered diffusely in both lungs, compatible with lung metastases. The imaging studies were consistent with metastatic, possibly synchronous bilateral, Wilms' tumor. Dr. Mueller, would you please present the imaging studies?

### Dagmar L. Mueller, MD (Pediatric Radiologist)

The abdominal ultrasound showed a large inhomogenous solid mass arising from the mid and lower pole of the left kidney (Fig. 1). This lesion measured approximately $7.9 \times 5.8 \times 7.4$ cm in the cephalocaudal, AP, and transverse planes, respectively. Abdominal CAT scan confirmed the presence of this lesion. The mass is surrounded by a thin rim of functioning tissue (Fig. 2), confirming the fact that we are dealing with an intrarenal tumor. The CAT scan also identifies a round hypodense lesion within the left renal vein, a finding consistent with tumor thrombus (Fig. 3). The inferior vena cava is normal.

Of particular interest are the changes noted within the right kidney, both demonstrated by ultrasonography and CAT scan. Both ultrasonography (Fig. 4) and CAT scan (Fig. 2) revealed, in the midportion of the right kidney, an apparent 3 cm well-defined solid mass. However, unlike the intrarenal lesion demonstrated in the left kidney, this lesion is of similar echotexture as the remaining renal cortex.

Finally the AP and lateral chest X-ray identified several pulmonary nodules identified particularly in the right lower lobe. These findings are consistent with pulmonary metastases. These lesions were confirmed on CAT scan of the chest.

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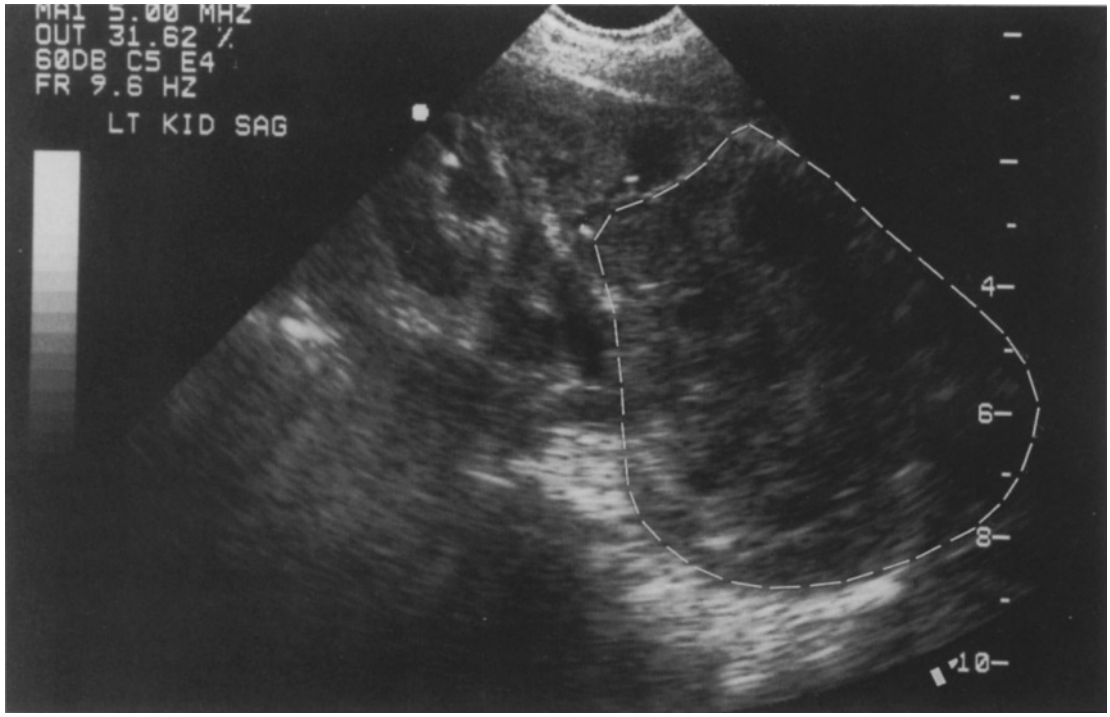


**Fig. 1.** Sagittal ultrasound of the left kidney demonstrates a large, solid, inhomogeneous mass (encircled) arising from the lower pole.

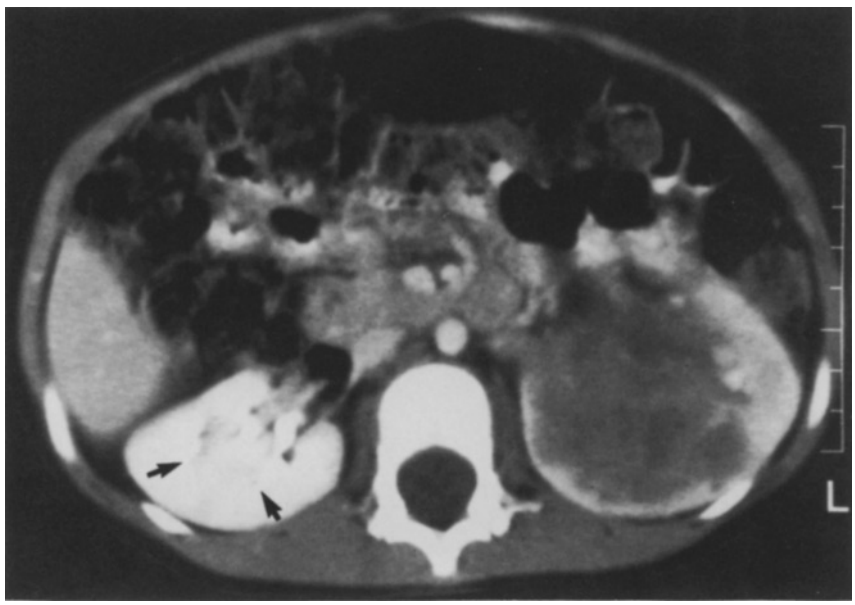


**Fig. 2.** Axial CAT scan depictes a large solid left intrarenal mass. Note the rim of functioning normal renal tissue surrounding the mass, confirming the intrarenal location of the lesion. The right kidney demonstrates a mass with normal contrast enhancement (arrows), similar to the remainder of the kidney.

**Ron M. Grant, MD (Pediatric Oncologist)**

Dr. Mueller, what would be your differential diagnosis for both renal lesions?

***Dr. Mueller.*** The lesion of the left kidney is very suspicious for a malignant tumor. Given the age of the child, the primary differential diagnosis to be considered

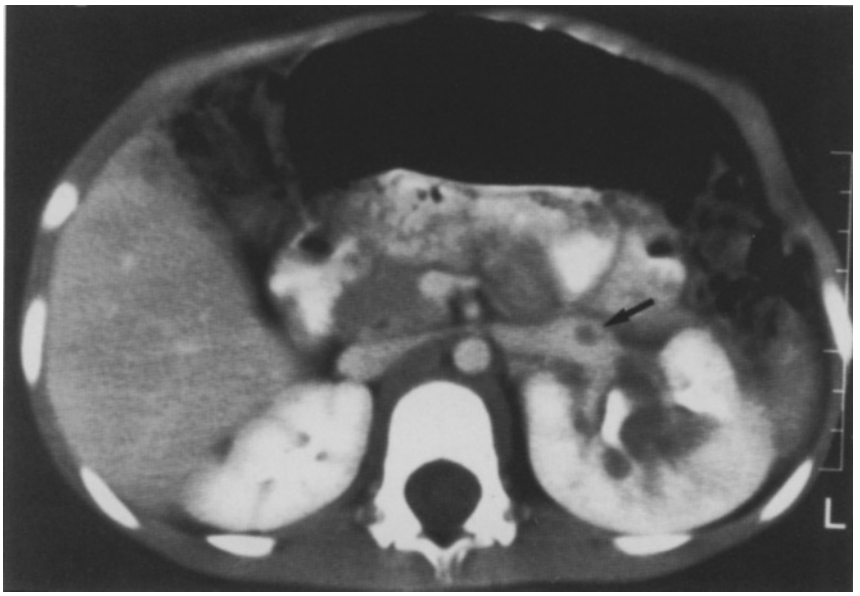


**Fig. 3.** Axial CAT scan showing the cephalad portion of the left Wilms' tumor. Note the rounded hypodensity (arrow), representing tumor thrombus, within the left renal vein.

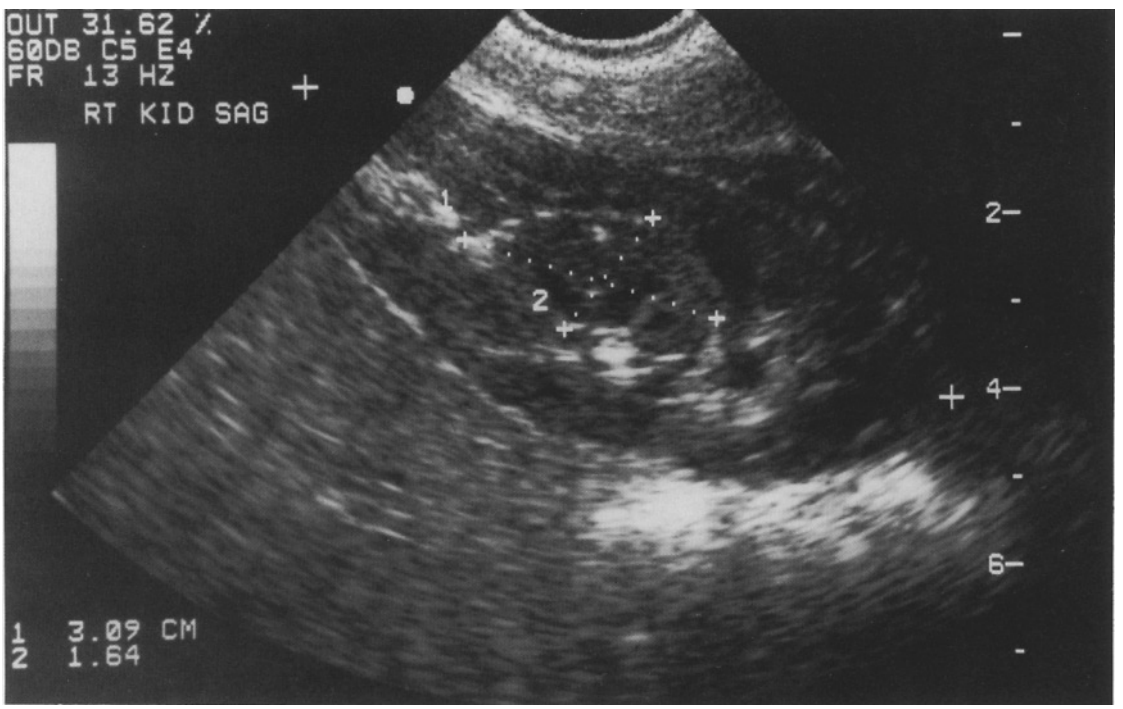


**Fig. 4.** Sagittal sonogram of the right kidney showing a 3.1 × 1.6 cm mass of similar echotexture to the remainder of the kidney.

is Wilms' tumor. No definite feature exists on imaging studies to differentiate Wilms' tumor from the other solid intrarenal tumors of childhood, such as clear cell sarcoma, rhabdoid tumor of the kidney, renal cell carcinoma, or mesoblastic nephroma. The right-sided lesion, however, is different as the echotexture of the mass looks very similar to that of the remaining renal cortex. A hypertrophied column of Bertin is therefore the most likely diagnosis, although bilateral Wilms' cannot be excluded.

***Dr. Coppes.*** Dr. Mueller, in retrospect, what imaging study would aid in differentiating between a column of Bertin from an intrarenal neoplasm?

***Dr. Mueller.*** Scintigraphy with a cortical imaging agent such as glucoheptonate or dimer captosuccinic acid (DMSA) and single positron emission computerized tomography (SPECT) could be useful in this differentiation. Normal functioning tissue as seen in hypertrophied column of Bertin would demonstrate uptake of the radiopharmaceutical, whereas an intrarenal tumor such as Wilms' would show a photon-deficient ''cold'' area.

***Dr. Coppes.*** Dr. Mueller, was the tumor thrombus within the left renal vein identified on abdominal CAT scan also detected on ultrasonography?

***Dr. Mueller.*** No. The tumor thrombus within the proximal left renal vein measured 5 mm on the enhanced CAT scan images. The epigastrium including the renal veins was obscured by bowel gas in this patient, a potential limiting feature in abdominal sonography. The inferior vena cava was readily evaluated by sonography and CAT scan in this patient and was clear. A few years ago, investigators from the National Wilms' Tumor Study (NWTS) group reported on the accuracy of different imaging modalities for tumor thrombus detection within the IVC [1]. Although this study revealed that ultrasound was better than CAT scan, the accuracy for ultrasound was only 54% as compared to 42% for CAT scan [1], demonstrating the limitations of both studies.

***Dr. Coppes.*** Let us return to the management of this patient, Dr. Anderson.

### Ron A. Anderson, MD (Pediatric Oncologist)

In view of these results, a laparotomy was suggested to the parents. Because of the suspicion of bilateral Wilms' tumor, the right kidney was explored first. Gerota's fascia was opened and two areas of thickening were palpated, one in the area previously indicated by imaging studies just superior to the hilum in the central portion of the renal parenchyma and another in the inferior pole. Biopsies were taken from both these regions with a ''TruCut'' (Travenol Laboratories) needle. Local hemostasis of the biopsy sites was ensured by temporarily compressing the biopsy sites with gauzes. On re-examination 10 minutes later, hemostasis appeared adequate. Frozen sections from both of the biopsy specimens revealed normal renal parenchyma with no evidence of tumor. In view of this result, only a left-sided radical nephrectomy was performed. Histopathologic examination revealed a favorable histology Wilms' tumor with extension in the renal vein. None of the removed lymph nodes showed evidence of metastatic involvement, i.e., this patient had a local stage II Wilms' tumor. However, due to pulmonary involvement (not histologically confirmed), the patient was classified as a stage IV Wilms' tumor. The immediate postoperative course was uncomplicated. After having obtained parental consent, the patient was registered on POG protocol #8650, i.e., NWTS-4, and randomized to regimen DD4A. As a consequence, she received actinomycin D (AMD), vincristine (VCR), and doxorubicin (DOX) for 54 weeks. In addition, bilateral whole lung radiotherapy to a dose of 1,200 cGy in eight fractions as per NWTS-4 protocol was administered. No complications were encountered during radiotherapy. On treatment, her blood pressure normalized, although the systolic blood pressure remained around the 95$^{th}$ percentile for her age ($\sim$110 mmHg). Two months into treatment, she was re-admitted to hospital because of ascites, elevated liver enzymes, and thrombocytopenia. The hepatopathy-thrombocytopenia [2] was thought to be secondary to AMD. The patient recovered with supportive therapy. Subsequent doses of AMD and DOX were reduced.

Three days following discharge for the hepatopathy-thrombocytopenia, a loud right flank bruit was noted on routine physical examination. It was also noted that both her systolic (128 mmHg) and diastolic (90 mmHg) blood pressures were markedly elevated, with a normal pulse and respiratory rate. Doppler ultrasound revealed large arteriovenous fistulae (AVF) in the single remaining right kidney. Subsequent renal angiography revealed the presence of two AVF's with large flow. Dr. Steed, would you please present the angiogram?

### Barrie L. Steed, MD (Interventional Radiologist)

As initial aortogram was performed with a pigtail catheter to roadmap the major vessels to the right kidney and to define the arteriovenous shunts (Fig. 5). The right main renal artery was large with two prominent branches to the mid upper pole and to the lower pole. Very dramatic arteriovenous shunting was demonstrated into the right renal vein and inferior vena cava from the upper pole of the right kidney. Although areas of normal vascularization of the kidney parenchyma were visualized, the dramatic shunting obscured vascular detail in other parts of the kidney. Subsequently, the right renal artery was selectively catheterized with a #4 French hockey stick type catheter using an angled Turomo guidewire. With contrast injection into the major branches, the exact anatomical location of the arteriovenous shunts in the upper pole and lower kidney were identified. The site of both lesions corresponded with the biopsy sites.

***Dr. Coppes.*** Are AVFs a frequent complication of renal needle biopsy, Dr. Donckerwolcke?

### Raymond A.M. Donckerwolcke, MD (Pediatric Nephrologist)

In general, renal biopsy in children has been extensively evaluated and found to be a relatively safe procedure. Microscopic hematuria or mild abdominal flank pain that disappears with 24–48 hours is a relatively common observation following biopsy, but generally it

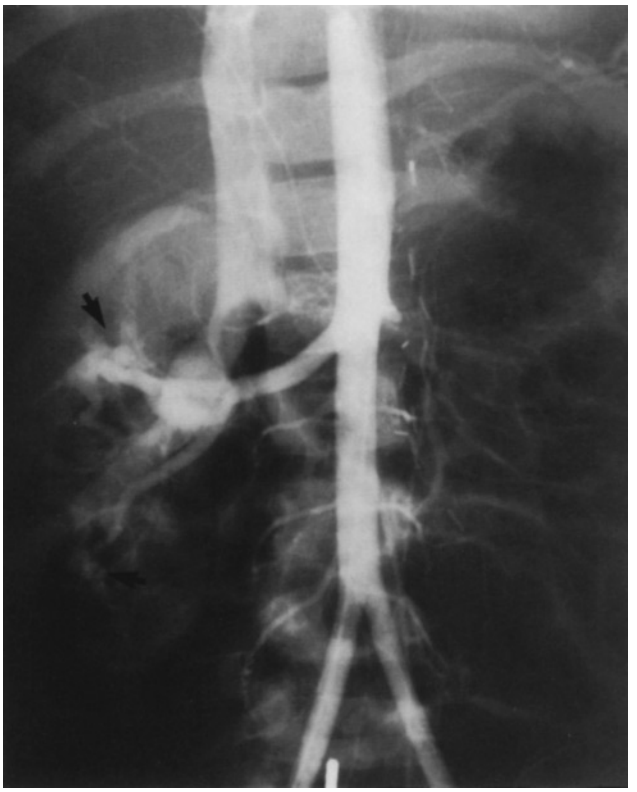

**Fig. 5.** Aortic angiogram obtained postleft nephrectomy and open right renal biopsies demonstrates two arteriovenous fistulae (arrows) resulting in immediate opacification of the inferior vena cava.

is not considered a complication. However, the incidence of more prolonged gross hematuria or passage of small clots, reported in 5–7% of biopsies, is regarded as a true complication. Occasionally (<2%), the hematuria can be so severe that a packed red cell transfusion is required. Rarely is a nephrectomy necessary to control bleeding. Other complications include renal infection and sepsis, renal infarction, ureteral obstruction, perirenal hematoma, transient increase in blood pressure, renal colic secondary to passage of clots, and arteriovenous fistula. The latter complication has been reported in 2–8% of patients undergoing a renal biopsy [3,4]. However, most of the literature reports on possible complications following percutaneous renal needle biopsy rather than open biopsy, and I suspect that the incidence of AVF following open renal biopsy is lower.

AVF may appear several days to 1 year following biopsy. It occurs more often in hypertensive patients and following penetration of the medulla [5]. The diagnosis is usually made based on the following clinical signs and symptoms: hematuria, hypertension, and the presence of a continuous bruit over the abdomen. However, definitive diagnosis is obtained by duplex Doppler ultrasonography, whereas the extent of the arterio-venous communication may be assessed by selective renal arteriography.

***Dr. Grant.*** What are the indications for intervention in renal AVFs?

***Dr. Donckerwolcke.*** Most AVFs appearing following renal biopsy are small and resolve spontaneously. Indication for correction of the anomaly include severe hypertension, deterioration of the renal function in the presence of a single kidney, and heart failure. Ultimately, treatment depends on the size and location of the lesion. Ligation of the afferent branch of the renal artery may be performed, but more recently, transcatheter intravascular embolization is being used [5,6].

***Dr. Anderson.*** Continued enlargement of the lesions was though to be likely with probable ensuing cardiac failure, and embolization of the AVFs was therefore recommended. Dr. Steed, would you please describe how you chose to embolize the AVFs?

***Dr. Steed.*** With the patient having only one kidney, our greatest concern was to preserve renal function as much as possible. To do this, the selective catheter was advanced via a percutaneous femoral artery catheterization, exactly to the origin of both AVFs. Spring coils 4 mm in diameter were used to embolize both arteriovenous shunts. The size of the coils was determined by measuring the size of the feeding vessels on cut film. Two coils were used at each location and total occlusion was assured by waiting for the AVF to occlude completely before final confirmatory angiography. Follow-up Doppler studies confirmed complete occlusion of both AVF's and the postembolization angiogram showed no evidence of arteriovenous shunting.

***Dr. Coppes.*** How did the patient fare following the embolization, Dr. Grant?

***Dr. Grant.*** Subsequent to the embolization, hypertension, which had been present prior to the procedure, worsened with systolic pressures ranging from 120–150 mmHg, diastolic pressures ranging from 80–100 mmHg. This has been managed with pharmacological intervention. Meanwhile, the glomerular filtration rate has remained normal at 147 ml/min/1.73m$^2$. Aside from compensatory renal hypertrophy, renal ultrasound has continued to demonstrate no structural abnormalities, in particular, no new AVFs. She remains free of tumor recurrence 3½ years following diagnosis, but still requires antihypertensive medication.

***Dr. Coppes.*** Dr. Donckerwolcke, this patient presented with hypertension that more or less resolved following nephrectomy. Subsequently, however, she redeveloped hypertension at the time of presentation of the AVFs and has remained hypertensive following the embolization of both AVFs. What mechanisms have contributed to the hypertension in this patient?

***Dr. Donckerwolcke.*** The incidence of hypertension in patients with newly diagnosed Wilms' tumors varies in different reported series from 25% to 63%. Increased renin production due to renal ischemia following com-

pression of the renal artery by the enlarged kidney or tumor has been proposed as a mechanism leading to hypertension in such patients [7,8]. Alternatively, the tumor itself might produce a pressor factor [9]. I believe that the hypertension noted at presentation in this patient might very well have been caused by renin, although no plasma levels are available to prove this hypothesis. The hypertension noted at the time that the patient presented with the two AVFs has a different etiology. This hypertension is caused by shunting of intrarenal blood flow, which results in parenchymal ischemia and subsequent stimulation of the renin-angiotensin-aldosteron-system (RAAS). Unfortunately, improvement of blood pressures after adequate treatment is not always observed. Finally, hypertension noted following the embolization of both AVFs might have been caused by renal damage due to the procedure, since intravascular embolization can result in a significant reduction of perfusion through certain renal segments, leading to hypertension. It should be noted that occasionally recurrent hypertension indicates tumor recurrence [10]. In this patient however, no evidence for local or metastatic tumor recurrence has been noted.

***Dr. Coppes.*** What is the prognosis for the function of this patient's remaining kidney?

***Dr. Donckerwolcke.*** According to this child's glomerular filtration rate (GFR), the remaining renal parenchyma demonstrates compensatory hypertrophy and functional adaptation. The latter is associated with increased glomerular capillary pressure and hyperfiltration, which may lead to progressive renal destruction [11]. In addition, this patient has hypertension resulting from renal damage following AVFs formation and subsequent embolization. Several studies have shown that the presence of one functional kidney following childhood disease increases the risk of the development of proteinuria and hypertension and a decrease in renal function during adulthood. For example, one recent study indicates that almost half of adults born with unilateral agenesis or nephrectomized in childhood and with an initially normal solitary kidney develop micro-albuminuria, whereas the GFR declines significantly with increasing follow-up [12]. Another study suggests that 10–15% of patients with unilateral renal agenesis will develop a serious decrease of their renal function [13]. In addition, focal glomerulosclerosis has been noticed in several patients following unilateral nephrectomy and radiotherapy for Wilms' tumor [14,15], a major role being attributed to radiotherapy [15]. However, not all patients with Wilms' tumor are at risk [16]. In this patient, intrarenal damage and hypertension will likely increase the risk of progressive destruction of the remaining glomeruli. It is uncertain whether restriction of dietary protein intake or reduction of the glomerular capillary pressure by converting enzyme inhibition could prevent the development of chronic renal disease in this child. However, control of blood pressure is imperative to prevent early deterioration of renal function.

***Dr. Coppes.*** Renal biopsy in patients with Wilms' tumor is infrequent because the NWTS group recommends upfront surgery, i.e., nephrectomy and investigators from the International Society of Paediatric Oncology (SIOP) advocate pre-nephrectomy chemotherapy without the need for tissue diagnosis. The NWTS approach allows accurate histopathologic confirmation of disease and tumor staging. Consequently, treatment can be tailored to the nature and extent of the disease at presentation. On occasion, needle biopsy may play a role, e.g., when the tumor is judged inoperable. While the SIOP Wilm's tumor regimens do not require tissue diagnosis before instituting treatment, investigators at the Hospital for Sick Children (HSC) in Toronto initiated a protocol to study the role of routine percutaneous needle biopsy prior to administering pre-nephrectomy chemotherapy [17]. At present, the HSC study is too small to provide adequate data with regard to the risks involved with the advocated approach. Here, we present one of the potential risks of diagnostic renal biopsy, which, of course, may go unnoticed in patients who subsequently undergo a nephrectomy of the biopsied kidney. Potentially, however, pretreatment renal biopsy may lead to renal dysfunction for patients undergoing nephron-sparing surgery, "the major benefit of preoperative chemotherapy" [17].

Renal biopsy is usually well tolerated, but several potential complications need to be considered. This patient illustrates one of the risks that must be taken into account if a diagnostic renal biopsy is considered. Other complications include the development of renal and perirenal hematomas, hematuria (which can be massive) and arteriocalyceal fistulas. There is also the risk of infection. All should be carefully weighed, particularly where there has already been tissue lost to nephrectomy or when such loss is anticipated.

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## Series Editor's Note

*Fistula* (Latin = pipe or reed) is used in medicine to indicate a pathologic channel communicating two internal structures, or from a deep focus to the surface. Often, the pathology is repulsive: a draining abscess or a fecal channel. It therefore seems unlikely that it would appear in the name of a hospital, but such was the case.

The British Commonwealth nations have had a tendency to use unambiguous terms in naming their institutions. Not for them, a *euphemistic* (Greek = use fair words) "Harmony Hill House" for an orphanage. No, it was—brutally—"The Home for Waifs and Strays," more seemly for an SPCA than an SPCC facility (Society for the Prevention of Cruelty to Animals and Children, respectively). This tendency toward straightforward talk is rather curious. At more or less the same time, many a *circumlocution* (Latin = round-about speech) was in use for body parts thought too indecent to be spoken aloud in polite company. For example, "leg"—whether of a table or a person—might become in Victorian Britain "nether support" or "nether extremity" (*nether* = below or down, from Old English *nither* = down).

Concerning the naming of institutions, this Proceedings comes from the Calgary Children's Hospital, but other pediatric institutions in Canada and England use "The Hospital for Sick Children." Although perhaps redundant in terminology, it leaves no doubt concerning the nature of the facility.

Clearly at the cloacal (Latin *cloaca* = drain or sewer, from the Greek *klyzein*, to cleanse) end of nomenclature is the name given the hospital founded in London in 1835 as "The Benevolent Dispensary for the Relief of the Poor Afflicted with Fistula, Piles and Other Diseases of the Rectum and the Lower Intestines"! The title was subsequently shortened to the sufficiently explicit "St. Mark's Hospital for Diseases of the Rectum and Colon," the world-renowned specialty institution.

Many hospitals are named after saints, of course, but why Mark was chosen for this particular instititon is not clear. Usually, it is an attribute, medical history, or the type of martyrdom that the saint suffered that connects the name with hospitals or specific medical entities.

St. Lucy is the patron saint of the blind and is usually depicted as carrying two eyes on a platter. Her life is full of legends, one of which states that she was devoted to a virginal life of good deeds and spurned all admirers. One of these men was persistent and to discourage him, she tore out her eyes. They were restored to her through a miracle, and she became the patron saint of the sightless. St. Agatha's is a rather similar story. She, too, spurned a determined suitor, who in revenge visited many tribulations on her, finally having her breasts cut off. Like Lucy, they were miraculously restored, and again like St. Lucy, St. Agatha is portrayed as carrying her two breasts on a platter. They are often confused with loaves of bread, so she is invoked by bakers as well as those afflicted with breast diseases. Legends aside, both these women were truly martyred in Sicily: Lucy in Syracuse and Agatha in Catania in the fourth and third centuries, respectively. Another martyr, St. Pancras, was beheaded in Rome for his Christian beliefs when only 14 years of age. Later, it is said that a perjurer in swearing falsely by St. Pancras touched the saint's tomb. St. Pancras' power caused the death of the false witness after making his arm cramp and become rigid. The saint, therefore, is not only called upon to assuage cramps but is also invoked when perjury or false witness is suspected.

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